JC06 Rec'd PCT/PTO U4 APR 2005

FORM PTO-1390 (Modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (REV 12-2004)

		TRANSMITTAL LETTER T	O THE UNITED STATES	attorney's docket number								
		DESIGNATED/ELECTED		081356-0239								
		CONCERNING A FILING		Unassigned 5.307								
	RNATIONAL AI	PPLICATION NO.		PRIORITY DATE CLAIMED 10/04/2002								
TITLE	OF INVENTIO	DN .	10/03/2003									
		ICIAL CHROMOSOME (HAC) VECTOR										
	ICANT(S) FOR Mitsuo OSHIM	URA, Motonobu KATOH, Kazuma TOMIZI	UKA, Yoshimi KUROIWA & Minoru KAKEDA									
Appli	cant herewith	submits to the United States Designated	/Elected Office (DO/EO/US) the following items and other in	nformation:								
1.	\boxtimes	This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.										
2.		This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.										
3.	_	This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.										
4.		The US has been elected (Article 31).										
5.	\boxtimes	A copy of the International Application a	s filed (35 U.S.C. 371(c)(2))									
		is attached hereto (required or	nly if not communicated by the International Bureau).									
		has been communicated by the	e International Bureau.									
		is not required, as the applicat	ion was filed in the United States Receiving Office (RO/US)									
6.	Ø	An English language translation of the Ir is attached hereto. has been previously submitted	nternational Application as filed (35 U.S.C. 371(c)(2)). under 35 U.S.C. 154(d)(4).									
7.		Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) are attached hereto (required only if not transmitted by the International Bureau). have been communicated by the International Bureau. have not been made; however, the time limit for making such amendments has NOT expired. have not been made and will not be made.										
8.		An English language translation of the a	mendments to the claims under PCT Article 19 (35 U.S.C.	371(c)(3)).								
9.		An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).										
10.		An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).										
ltem	s 11 to 20 be	low concern other document(s) or inform	nation included:									
11.	×	An Information Disclosure Statement un	der 37 CFR 1.97 and 1.98.									
12.		An assignment document for recording.	A separate cover sheet in compliance with 37 CFR 3.28 a	and 3.31 is included.								
13.	\boxtimes	A preliminary amendment.										
14.	\boxtimes	An Application Data Sheet under 37 CFF	R 1.76.									
15.		A substitute specification.	·									
16.		A power of attorney and/or change of a	ddress letter.									
17.	\boxtimes	A computer-readable form of the sequer	nce listing in accordance with PCT Rule 13 ter.2 and 37 CFR	1.821 – 1.825								
18.		A second copy of the published internati	onal application under 35 U.S.C. 154(d)(4).									
19.		A second copy of the English language t	ranslation of the international application under 35 U.S.C. 1	54(d)(4).								
20.	\boxtimes	Other items or information: Microorgania	sm Deposit receipt, Translation of Receipt, Declaration, Pe	tition to Accept Color Photographs, PCT/IB/308; PCT/IB/30								
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JC06 Rec'd PCT/PTO 04 APR 2005

US. APPLICATION, NO. (H I	753	ከኃበ		INTERNATIONAL APPLICATION NO. PCT/JP2003/012734	•	ATTORNEYS DO 081356		R _					
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fraction thereof.													
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		mishing the oath	h or declara	tion later than 30 months from the	earliest daim	ed priority date	\$	130.00					
(37 CFR 1.492(e)	}			AND CO CYTO	1 -	NATE .	-						
CLAIMS		NUMBER	FILED	NUMBER EXTRA		RATE	\$						
Total Claim		66	- 20 =	46	x\$.	50.00	\$	2300.00					
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			\$	4940.00									
☐ Applica	Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by ½.												
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Fol	ley & Lan	dner LLP				Stephen A. Bent							
Cus	stomer N	umber: 2242	NAME										
						29,768							
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			4. 2005										



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Mitsuo OSHIMURA et al.

Title:

HUMAN ARTIFICIAL CHROMOSOME (HAC) VECTOR

Int'l. Appl.

PCT/JP2003/012734

No.:

Int'l. Filing

October 3, 2003

Date:

Examiner:

Unassigned

Art Unit:

Unassigned

PETITION TO ACCEPT COLOR PHOTOGRAPHS UNDER 37 CFR 1.84

Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

Sir:

In accordance with 37 CFR 1.84(a)(2), Applicants petition for the acceptance of Figs. 3, 4a, 4b, 6, 7a, 7b, 9, 10, 13, 14, 15a, 15b, 17, 18a, 18b, 20a, 20b, 21, 22a and 22b(photographs) to be entered in the above-captioned application.

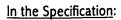
In support thereof, Applicants submit:

- I) A fee in the amount of \$130.00 as is set forth under 37 CFR 1.17(h);
- II) Three (3) sets of each figure set forth above;
- III) An amendment to the specification indicating that the application contains color photographs.

04/08/2005 SNAJARRO 00000019 10530207

09 FC:1464

130.00 OP



On page 1, directly beneath the title, please insert the following:

--The application contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.--

REMARKS

Fig. 3 is a photograph showing the results of southern blot analysis indicating the deletion of the distal region of the long arm in the puromycin resistant DT40 clone, or the introduction of an artificial telomere sequence in a site-specific manner.

Figs. 4a and 4b are photographs showing the results of FISH analysis indicating the deletion of the distal region of the long arm in the puromycin resistant DT40 clone. Figure 4a shows a human chromosome 21 (arrow) retained in the DT40 cell, and Figure 4b shows a human chromosome 21 fragment (arrow) from which the long arm has been deleted.

Fig. 6 is photographs showing the results of southern blot analysis (A) and PCR analysis (B) used to screen the blasticidin resistant DT40 clone for homologous recombinants (clones in which the loxP sequence was introduced into human chromosome 21 in a site-specific manner).

Fig. 7a and 7b are photographs showing the results of FISH analysis indicating the retention of a human chromosome 21 (fragment) in the blasticidin resistant CHO-K1 clone. Figure 7a shows a full-length (entire) human chromosome 21 before telomere truncation and Figure 7b shows a human chromosome 21 fragment from which the distal region of the long arm has been deleted.

Fig. 9 is a fluorescence microscope photograph showing GFP expression in the G418 resistant CHO-K1 clone.

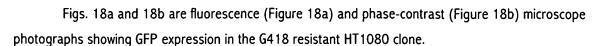
Fig. 10 is a photograph showing the results of southern blot analysis indicating the occurrence of sitespecific recombination in a loxP sequence in the G418 resistant CHO-K1 clone.

Fig. 13 is a photograph showing the results of southern blot analysis indicating the deletion of the distal region of the short arm in the hygromycin resistant DT40 clone, or the introduction of an artificial telomere sequence in a site-specific manner.

Fig. 14 is a photograph showing the results of PCR analysis indicating the deletion of the distal region of the short arm in the hygromycin resistant DT40 clone, or the introduction of an artificial telomere sequence in a site-specific manner.

Figs. 15a and 15b are photographs showing the results of FISH analysis indicating the deletion of the distal region of the short arm in the hygromycin resistant DT40 clone. Figure 15a shows a human chromosome 21 (arrow) devoid of the long arm retained in the DT40 cell, and Figure 15b shows a human chromosome 21 fragment (arrow) from which the long and short arms have been deleted.

Fig. 17 is a photograph showing the results of FISH analysis indicating the retention of a human chromosome 21 fragment (arrow) in the blasticidin resistant HT1080 cell clone.



Figs. 20a and 20b are photographs showing the results of FISH analysis indicating the retention of a human chromosome 21 fragment in the drug resistant E14 cell clone. Figure 20a shows a chromosome fragment (arrow) devoid of the distal region of the long arm, and Figure 20b shows a chromosome fragment (arrow) from which the distal region of the short arm has been further deleted.

Fig. 21 is a photograph showing the results of FISH analysis indicating the retention of a human chromosome 21 fragment (arrow) in the drug resistant hiMSC cell clone.

Figs. 22a and 22b are fluorescence microscope photographs showing GFP expression (Figure 22a) and staining with anti-beta tubulin antibody (Figure 22b) when ES cells retaining HAC were induced to differentiate into nerve cells *in vitro*.

Respectfully submitted,

Stephen A. Bent Attorney for Applicant

Registration No. 29,768

Date 4 April 2009

FOLEY & LARDNER LLP Customer Number: 22428 *22428*

22428

PATENT TRADEMARK OFFICE

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Mitsuo OSHIMURA et al.

Title:

HUMAN ARTIFICIAL CHROMOSOME (HAC) VECTOR

Int'l. Appl. No.:

PCT/JP2003/012734

Int'l. Filing

October 3, 2003

Date:

Examiner:

Unassigned

Art Unit:

Unassigned

DECLARATION

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

I declare:

- 1. A deposit of the microorganism identified as SC20, of Accession number FERM BP-7583, was made at the International Patent Organism Depositary, National Institute of Advanced Industrial Science and Technology, AIST Tsukuba Central 6, 1-1, Higashi 1-Chome, Tsukuba-shi, Ibaraki-ken 305-8566 Japan and accepted under the provisions of the Budapest Treaty for patent purposes.
 - 2. The deposit having Accession number FERM BP-7583 was made on May 9, 2001.
- 3. All restrictions on the availability to the public of the culture deposited will be irrevocably removed upon the granting of a patent from the above-identified application.
 - 4. The deposit will be replaced if viable samples cannot be dispensed by the depository.
- 5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or

imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Signed this 4th day of April 2005,

Name: Stephen A. Bent

Reg. No. 29,768

Applicants' Representative

INTERNATIONAL FORM

BUDAPEST TREATY ON THE INTERNATIO-NAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT

issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page.

TO DEPOSITOR:

Name:

KIRIN BEER KABUSHIKI KAISHA

Representative: Koichiro ARAMAKI

Address:

10-1, Shinkawa 2-chome, Chou-ku, Tokyo, Japan

I. IDENTIFICATION OF MICROORGANISM

Identification Reference Given by the Depositor:

Accession Number:

SC20

FERM BP-7583

II. A SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC POSITION

The microorganism identified under I above was accompanied by a document stating the following item(s).

- A Scientific Property
- Taxonomic Position

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts the microorganism identified under I above, which was received on May 9, 2001.

(date of the original deposit)

IV. RECEIPT OF REQUEST FOR TRANSFER

This International Depositary Authority received the microorganism under I above on (date of the original deposit), and received on a request for transfer from the original deposit to the deposit under the Budapest treaty.

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: International Patent Organism Depositary

National Institute of Advanced Industrial Science and Technology

Representative: Dr. Yasuhiko KOMATSU, Director (sealed)

Address:

AIST Tsukuba Central 6, 1-1, Higashi 1-Chome, Tsukuba-shi,

Ibaraki-ken 305-8566 Japan

Date: May 9, 2001